

### REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on May 23, 2003 and requests consideration of the following remarks.

#### §103 Rejection of the Claims

**Claims 1, 3, 4, 11, 13, 14, 26-29, 34 and 35 were rejected under 35 U.S.C. § 103(a) as being unpatentable over the Rephaeli (U.S. Pat. No. 5,939,455).** This rejection is respectfully traversed.

The present claims are directed to the use of a group pyranylindanoacetic acids, including the non-steroidal anti-inflammatory agent (NSAID) etodolac, to reduce the viability of cancerous bone marrow cells. The claims are based on the unexpected discovery that etodolac has a potent inhibitory affect on the type of cancerous cells that characterize myelomas.

The Rephaeli '455 patent discloses and claims a method to augment the therapeutic activity of large genes including an "oxyalkylene containing compound, butyric acid, a butyric acid salt or butyric acid derivatives," Col. 1, lines 59-63; Col. 4, lines 54-60. The '455 patent discloses that the  $\beta$ -oxidation of these active agents can be inhibited with NSAIDs, including etodolac. Col. 4, lines 23-27. The Examiner is urged to consider that the patent does not ascribe any therapeutic effect against the cancer cells to the NSAID – these are used to protect the active ingredient from degradation.

While the present claims employ open "comprising" language, the Examiner is requested to consider that all of the claims recite that the compound of formula I, *e.g.*, the etodolac or analog, or 1-R(-)-etodolac is itself administered in an amount that is per se effective to reduce the viability of cancerous bone marrow cells, regardless of what other agent may be included in the treatment including any of the butyric acids or "cytotoxic agents" disclosed by the '455 patent.

Furthermore, the Examiner is requested to note that in the '455 patent, claim 25 is drawn to a method of protecting normal stem cells in a patient by blocking their proliferation, while the additional "cytotoxic agent" and the butyric acid derivative also kill cancerous cells. See, Col.6, lines 26-50 where this "effect" is set forth in more detail. In contrast, the present invention is recited to reduce the viability of cancerous MM cells, while maintaining the viability of normal

bone marrow cells (which includes a much wider population than “stem cells”), not inducing their “growth arrest,” as is accomplished by the ‘455 patent.

Thus, in order for one of ordinary skill in the art to find the presently-claimed invention obvious in view of the full disclosure of the ‘455 patent, the art worker would be required to ignore the explicit teachings that the  $\beta$ -oxidation inhibitor, such as etodolac, including R(-) etodolac, functions to protect the active agent from degradation and use it as the active agent, to inhibit multiple myeloma cells. It is respectfully submitted that there is no teaching in the ‘455 patent that would reasonably teach the art worker to believe that this should even be attempted, much less that it would be accomplished. Furthermore, there is even less in the cited art that would lead the art worker to believe that the  $\beta$ -oxidation inhibitor, such as etodolac, would itself maintain the viability of normal marrow cells while inhibiting the viability of the cancerous cells, as recited by claim 26.

Therefore, it is respectfully submitted that the present claims are not obvious in view of the ‘455 patent, and withdrawal of this rejection is respectfully requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6968) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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By their Representatives,

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Date Sept. 23, 2003

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 23rd day of August, 2003.

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